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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,282	11/10/2003	Samuel Chackalamannil	CV01185K1X	4919

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUYNH, CARLIC K	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,282	CHACKALAMANNIL ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-16,19-27 and 29-43* is/are pending in the application.

4a) Of the above claim(s) *1-8,11-16,19-27 and 29-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-43* is/are rejected.

7)☒ Claim(s) *28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on September 21, 2007 is acknowledged.

Status of the Claims

1. Claims 1-8, 11-16, 19-27 and 29-43 are pending in the application, with claims 1-8, 11-16, 19-27, and 29-39 having been withdrawn from consideration, with claims 9-10, 17-18, and 28 having been cancelled, and with new claims 40-43 having been added, in an "Amendment – After Non-Final Rejection" filed on September 21, 2007. Accordingly, claims 40-43 are being examined on the merits herein.

It is noted that claims 1-8 are withdrawn and not "1-18" as stated in the "Remarks/Arguments" filed on September 21, 2007. Moreover, Applicants have not cancelled claim 28 from the claims but rather merely stated claim 28 was cancelled in the "remarks/arguments", see "Amendment – After Non-Final Rejection" filed on September 21, 2007, with respect to the "Status of the Claims". However, to expedite prosecution, claim 28 is considered cancelled.

Response to Arguments

2. Applicants' amendment, see "Amendment – After Non-Final Rejection" filed on September 21, 2007, with respect to the "Specification" have been fully considered and are found persuasive. Examiner had objected the abstract for containing legal phraseology, namely "said" and for being greater than a paragraph in length. Applicants have amended the abstract to

remove "said" and to one paragraph in length. Thus the Objection to the Specification has been withdrawn in light of the amendments.

3. Applicant's amendments, see "Amendment-After Non-Final Rejection" filed on September 21, 2007, with respect to "Rejections under 35 U.S.C. § 112, first paragraph" to claims 9-10, 17-18, and 28 have been fully considered and are persuasive. Applicants have cancelled claims 9-10, 17-18, and 28 and have added new claims 40-43. It is noted that new claims 40-43 are limited to the treatment of only acute coronary syndrome. Thus, the Rejections under 35 U.S.C. § 112, first paragraph to claims 9-10, 17-18, and 28 have been withdrawn in light of the amendments.

4. Applicant's amendments, see "Amendment-After Non-Final Rejection" filed on September 21, 2007, with respect to "Rejections under 35 U.S.C. § 102" to claims 9-10 have been fully considered and are persuasive in part. Applicant argues that Chackalamannil et al. (US 6,063,847) teach the ring Q, R is $-NR^{16}COOR^{16a}$, where within this group, the carbamates are limited to secondary amine carbamates because R^{16} is not hydrogen. Moreover, Applicants have cancelled claims 9-10. Examiner agrees that Chackalamannil et al. does not explicitly teach the claimed compound. However, Examiner argues that because R^{16} can be alkyl, namely CH_3, the compound of Chackalamannil et al. would be an **obvious** homolog to the claimed compound and the compound in new claim 40. Thus, the Rejections under 35 U.S.C. § 102 to claims 9-10 have been withdrawn in light of the amendments.

It is noted that under the heading of "Rejections under 35 U.S.C. § 102" of page 7 of the Office Action filed on March 23, 2007, claims 9-10 are indeed rejected under 35 U.S.C. § 102,

not 35 U.S.C. § 103(a). Examiner acknowledges the telephone conference with Applicants' Representative to clarify the rejection was indeed under 35 U.S.C. § 102 to claims 9-10.

5. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on September 21, 2007, with respect to "Obviousness Type Double Patenting" to claim 9 have been fully considered and are persuasive in part.

Applicants argue that claim 1 of Chackalamannil et al. (US 6,063,847) defines the ring Q, R is $-NR^{16}COOR^{16a}$, where within this group, the carbamates are limited to secondary amine carbamates because R^{16} is not hydrogen. Examiner agrees that the compound of claim 1 of Chackalamannil et al. does not explicitly teach the instant claimed compound. However, Examiner argues that because R^{16} can be alkyl, namely CH_3, the compound in claim 1 of Chackalamannil et al. would be an **obvious** homolog to the instant claimed compound and the instant compound in new claim 40.

Applicants argue that Chackalamannil et al. (US 2006/0079684 or 11/243,708) discloses a genus of compounds in which the common member of the left hand- and center- rings is substituted, in contrast to the compound of new claim 40, in which that common ring member is unsubstituted. Examiner agrees and further states that in the compound of Chackalamannil et al., R^3 is not H and thus is not the instant compound.

Applicants argue that Thiruvengadam et al. (US 2006/0173189 or 11/330,936) is directed to synthesizing the compound of Claim 40 and is not the same as new Claim 40, which is directed to a method of treating acute coronary syndrome. Examiner agrees because claim 1 of Thiruvengadam et al. is not directed at a method of treating acute coronary syndrome.

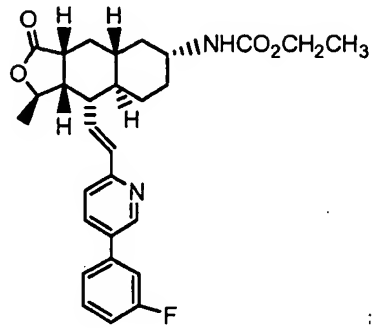
Applicants argue that claim 18 of Chackalamannil et al. (US 6,063,847) defines the ring Q, R is $-NR^{16}COOR^{16a}$, where within this group, the carbamates are limited to secondary amine carbamates because R^{16} is not hydrogen. Examiner agrees that the compound of claim 18 of Chackalamannil et al. does not explicitly teach the instant claimed compound. However, Examiner argues that because R^{16} can be alkyl, namely CH_3, the compound in claim 18 of Chackalamannil et al. would be an **obvious** homolog to the instant claimed compound and the instant compound in new claim 40. Moreover, Examiner also argues that claim 18 of Chackalamannil et al. is directed at a method of treating myocardial infarction. As evidenced by Gerlitz et al. (US 2003/0022354), myocardial infarction is an acute coronary syndrome (page 2, paragraph [0016]).

Applicants argue that claim 9 of Chackalamannil et al. (US 6,326,380) is directed to a set of bicyctic compounds that are in distinction to the tricyclic compound of instant claim 40. Examiner agrees because the compounds in claim 9 of Chackalamannil et al. are not the same compounds of the instant invention.

Applicants argue that claims 45 and 51 of Barbeau (US 2005/0130975 or 10/987,959) are directed to a subject matter that is unrelated to the instant invention. Examiner agrees that the subject matter of claims 45 and 51 of Barbeau is unrelated to the instant invention.

Applicants argue that claim 1 of Veltri et al. (11/613,450) is directed at a method of preventing a condition associated with coronary arterial bypass graft surgery comprising administering an effective amount of at least one thrombin receptor antagonist to a subject of said surgery. Examiner agrees in part. Examiner had made an incomplete listing of the claims of Veltri et al. when making this Obviousness Type Double Patenting rejection. Claims 1-4, 9,

and 16 of Veltri et al, directed at a method of treating acute coronary syndrome using a compound of the formula,



is the same invention as the instant invention.

Thus, the Obviousness Type Double Patenting rejections to claim 9 under patent applications Chackalamannil et al. (11/243,708), Thiruvengadam et al. (11/330,935), and Barbeau (10/987,959) and under Chackalamannil et al. (US 6,326,380) have been withdrawn in light of the amendments. The Obviousness Type Double Patenting rejections to claim 9 under Chackalamannil et al. (US 6,063,847) and patent application Veltri et al. (11/613,450) have been maintained.

6. Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection. The following new ground(s) of rejection to new claim 2 is used herewith.

Specification

7. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means"

and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the instant application contains legal phraseology, namely "said". Additionally, the abstract of the instant application contains two paragraphs. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

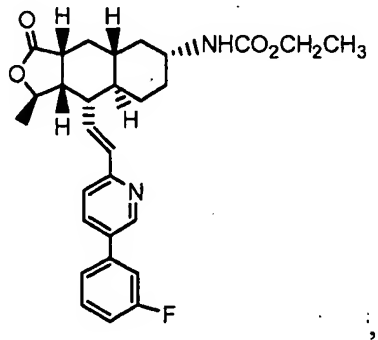
8. Claims 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chackalamannil et al. (US 6,063,847) in view of Gerlitz et al. (US 2003/0022354).

Chackalamannil et al. teach thrombin receptor antagonists according to formula I, and more specifically, compounds of formula IA, which are homologous to the compounds of the

instant claimed invention, when X is O, Y is =O, R^1 is methyl, R^3, R^8, R^9, R^{10}, and R^{11} are all hydrogen, B is -CH=CH-, Het is optionally substituted pyridyl, and R is $-NR^{16}COOR^{16a}$, where R^{16} and R^{16a} are alkyl, which can be CH_3 or CH_2CH_3 (column 2, formula I; and column 4, formula IA). It is noted that when R^{16a} is CH_3, the compound of Chackalamannil et al. is considered an obvious homolog of the instant compound in instant claim 40, i.e., they differ only by a CH_2 group. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950).

Furthermore, Chackalamannil et al. teach a method for treating acute coronary syndrome as well as other cardiovascular diseases such as myocardial infarction (column 5, line 38). It is noted that Gerlitz et al. teach a method of treating acute coronary syndrome such as myocardial infarction (page 2, paragraph [0016]). Thus, Gerlitz et al. disclose myocardial infarction is an acute coronary syndrome.

Regarding the bisulfate salt of the compound,



in instant claim 41, Chackalamannil et al. teach pharmaceutically acceptable salts of the compounds. Since bisulfate is a well known pharmaceutically acceptable salt, it would be obvious that the compounds of Chackalamannil et al. teach the bisulfate salt of the instant compound.

Chackalamannil et al. does not teach aspirin and clopidogrel.

Gerlitz et al. teach a method of treating acute coronary syndrome such as myocardial infarction comprising administering an anti-platelet agent, namely aspirin or clopidogrel (page 2, paragraphs [0016] and [0029]).

Accordingly, absence the showing of unexpected results, it would have been obvious to a person of skill in the art at the time of the invention to employ the composition of Chackalamannil et al. to include aspirin and clopidogrel because the compounds of Gerlitz et al. teach aspirin and clopidogrel and according to Gerlitz et al., aspirin and clopidogrel can be used to treat acute coronary syndrome.

The motivation to combine the compounds of Chackalamannil et al. to the compounds of Gerlitz et al. is that the compounds of Gerlitz et al. are aspirin and clopidogrel compositions and that such compositions treat acute coronary syndrome.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Regarding clopidogrel bisulfate as recited in claim 43, Gerlitz et al. teach a method of treating acute coronary syndrome such as myocardial infarction comprising administering an anti-platelet agent, namely aspirin or clopidogrel (page 2, paragraphs [0016] and [0029]). Compounds are routinely administered in pharmaceutically acceptable salt forms of those compounds and since bisulfate is a well known pharmaceutically acceptable salt form, it would be obvious that Gerlitz et al. teach clopidogrel bisulfate.

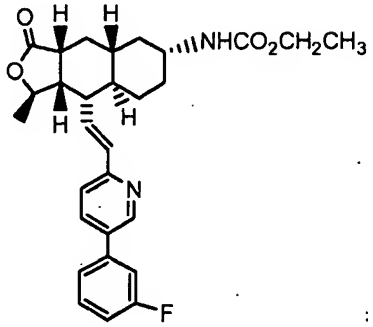
Double Patenting

Statutory-Type

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9. Claim 40 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 25, 28, 33, 38, 43, 48, 53, and 58 of Chackalamannil et al. (US 7,304,078) as evidenced by Gerlitz et al. (US 2003/0022354). The conflicting claims are both directed at a method of treating myocardial infarction comprising administering a compound of the formula,



or pharmaceutically acceptable salts thereof. As evidenced by Gerlitz et al., myocardial infarction is a specific type of acute coronary syndrome (page 2, paragraph [0016]). Thus myocardial infarction is a specific type of acute coronary syndrome and any method that is directed to treating myocardial infarction can also treat acute coronary syndrome.

Obviousness-Type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

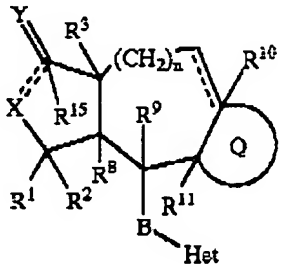
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 40 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 18 of Chackalamannil et al. (U.S. Patent 6,063,847) as evidenced by Gerlitz et al. (US 2003/0022354).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of Chackalamannil et al. (U.S. Patent 6,063,847) is directed at a composition of formula I, which is homologous the composition used in a method of treating a therapeutic condition in the instant claim 40.

Moreover, claim 1 of Chackalamannil et al. teach thrombin receptor antagonists according to formula,



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which are homologous to the compounds of the instant claimed invention, when X is O, Y is =O, R^1 is methyl, R^3, R^8, R^9, R^{10}, and R^{11} are all hydrogen, B is -CH=CH-, Het is optionally substituted pyridyl, and R is $-NR^{16}COOR^{16a}$, where R^{16} and R^{16a} are alkyl, which can be CH_3 or CH_2CH_3. It is noted that when R^{16a} is CH_3, the compound in claim 1 of Chackalamannil et al. is considered an obvious homolog of the instant compound in instant claim 40, i.e., they differ only by a CH_2 group. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to

prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950).

Thus the composition is not patentably distinct between Chackalamannil et al. (US 6,063,847) and the instant application.

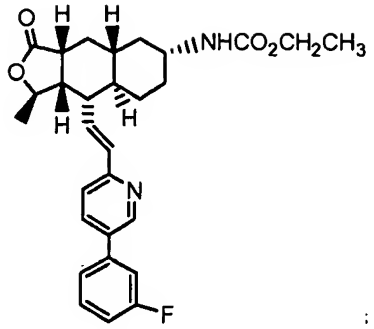
Furthermore, Claim 18 of Chackalamannil et al. (US 6,063,847) is directed to a method of treating myocardial infarction comprising administering the compounds of claim 1.

As evidenced by Gerlitz et al., myocardial infarction is a specific type of acute coronary syndrome (page 2, paragraph [0016]). It would be obvious the method of treating myocardial infarction comprising administering compounds of claim 1 is the method of treating acute coronary syndrome comprising administering compounds of claim 1.

Thus, the method of treating acute coronary syndrome is not patentably distinct between Chackalamannil et al. (US 6,063,847) and the instant application.

11. Claim 40 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 9, and 16 of copending Application Veltri et al. (US Serial Number 11/613,450).

The claims of Veltri et al. are directed at a method of treating a condition associated with cardiopulmonary bypass surgery, in which the condition may be acute coronary syndrome, comprising administering the compound of the formula,



Thus, it would be obvious that the method of Veltri et al. may be a method of treating acute coronary syndrome. As such, the method of treating acute coronary syndrome is not patentably distinct between Veltri et al. (11/613,450) and the instant application.

This is a provisional double patenting rejection since the conflicting claims have not been patented.

Conclusion

12. No claims are allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER

ckh